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Relationship between Serum Lipid Values and Atherosclerotic Burden in the Proximal Thoracic Aorta

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Abstract

BACKGROUND—We conducted a cross-sectional analysis in a population-based cohort to compare the strength of the associations among various lipid parameters and the presence of atherosclerotic plaque (AP) in the proximal thoracic aorta.

METHODS—As part of Aortic Plaques and Risk of Ischemic Stroke (APRIS) study, 464 subjects were studied (mean age 69.1±9.0, 251 males and 213 females), including 255 patients with first ischemic stroke and 209 stroke-free controls. Presence and thickness of AP were assessed by transesophageal echocardiography. Measured lipid parameters included total cholesterol, triglycerides (TG), LDL, HDL, and non-HDL cholesterol, lipoprotein (a), apolipoprotein (Apo) B and A-I levels with their ratio.

RESULTS—Overall, AP was detected in 326 subjects (70.4%) and 37.6% of these subjects (n=174) had AP ≥4mm. After adjusting for other significant predictors of atherosclerosis, HDL cholesterol level and Apo B/A-I ratio emerged as the strongest predictors of any AP ($p<0.001$ and $p=0.004$, respectively), followed by individual Apo B ($p=0.015$) and A-I ($p=0.016$) levels, TG ($p=0.027$) and non-HDL cholesterol level ($p=0.021$). Total and LDL cholesterol levels were not significant predictors for any AP ($p=0.273$ and $p=0.081$, respectively). HDL cholesterol level ($p=0.008$) and Apo A-I ($p=0.006$) were significant predictors of AP ≥4mm. Similar trends were observed after exclusion of subjects on cholesterol lowering drugs.

CONCLUSIONS—HDL cholesterol level and Apo B/A-I ratio, but not total or LDL cholesterol levels, were strongly associated with degree of proximal aortic atherosclerosis.

Keywords

atherosclerosis; cardio-aortic embolism; lipids; apolipoproteins; risk factors

Background

Current lipid lowering guidelines recommend that therapy for preventing and managing cerebrovascular and cardiovascular disease (CVD) be targeted primarily at low-density lipoprotein (LDL) cholesterol.(1) Clinical studies such as REVERSAL (Reversal of Atherosclerosis with Aggressive Lipid Lowering) showed that lowering LDL reduces the plaque burden in the coronary arteries.(2) (3,4) However, LDL may not be an optimal predictor of future cardiovascular events. High-density lipoprotein (HDL) cholesterol, which is known to be strongly, independently, and inversely associated with CVD, may be a new potential target.(5) Emerging data suggest that HDL cholesterol may be more predictive of actual atherosclerotic burden than LDL cholesterol.(6,7) A recent post-hoc analysis from Treating to New Targets (TNT) Study showed that the HDL cholesterol level in patients receiving statins was predictive of major cardiovascular events, even among study subjects with LDL cholesterol levels below 70 mg/dl.(8)

In addition, determining the level of HDL apolipoprotein component (apolipoprotein AI) and its ratio to apolipoprotein B in atherogenic lipoproteins (Apo B/A-I ratio) could theoretically improve the prediction of atherosclerotic burden. Large-scale studies, such as AMORIS (Apolipoprotein related MORTality RiSk) and INTERHEART,(9,10) have unambiguously shown that the Apo B/A-I ratio is a robust predictor for future CVD events.

The measurement of thoracic aortic atherosclerotic plaque (AP) thickness by transesophageal echocardiogram (TEE) is a well-validated technique for evaluating the progression of atherosclerosis,(11,12) and AP is an increasingly recognized stroke risk factor, particularly among the elderly (13,14). A plaque thickness cutoff of 4 mm is widely acknowledged as clinically relevant for risk stratification. The French Aortic Plaque in Stroke (FAPS) study indicated that not only that plaque thickness was associated with stroke risk, but also that the risk was significantly greater in those with a plaque thickness ≥ 4 mm. (14) The OR for stroke in patients with plaques < 1 mm was 1.0; for 1- to 3.9-mm plaques, it was 3.9; and for plaques ≥ 4 mm, the OR was 13.8. This cutoff for risk stratification has subsequently been used in numerous studies.(15–17)

As part of the NINDS-funded Aortic Plaques and Risk of Ischemic Stroke (APRIS) study, we conducted a cross-sectional analysis in a population-based sample to compare the strength of the associations among various lipid parameters and the presence and thickness of AP in the proximal thoracic aorta.

Methods

The Aortic Plaque and Risk of Ischemic Stroke (APRIS) study, in which TEE was performed in patients with acute ischemic stroke and in matching control subjects, affords a rare opportunity to examine risk factors associated with aortic arch atherosclerosis. All participants come from the Northern Manhattan area of the New York City.

The participants in the APRIS study were recruited from a larger population-based cohort study among residents of northern Manhattan (the Northern Manhattan Study [NOMAS]). The methods of subject recruitment and enrollment in NOMAS have been described in previous publications.(18) Since aortic AP is rarely observed at a younger age, participants in APRIS were limited to those ≥ 55 years of age. The present report is based on 255 patients with first ischemic stroke consecutively referred for TEE, and 209 stroke-free controls drawn from the NOMAS cohort and matched to cases by age, sex and race-ethnicity.

The study was approved by the Institutional Review Board at Columbia-Presbyterian Medical Center. All participants gave consent directly or through a surrogate when appropriate.

Baseline evaluation was performed at enrollment as previously reported.(18) Standard techniques were used to measure blood pressure, height, weight, and fasting glucose. Fasting lipid panels (including total cholesterol, LDL, HDL, and triglycerides) along with lipoprotein (a), apo B and apo AI were measured with a Hitachi 705 automated spectrometer (Boehringer).

Cardiovascular risk factors were collected by direct interview using standardized questions adapted from the Centers for Disease Control and Prevention Behavioral Risk Factor Surveillance System or by medical record review.(19) Hypertensive status was defined as a systolic blood pressure recording ≥ 140 mm Hg or a diastolic blood pressure recording ≥ 90 mm Hg based on the mean of the 2 readings of the blood pressure measurements, a patient's self-report of a history of hypertension, or antihypertensive medication use. A history of diabetes mellitus was defined by a patient's self-report of such a history, insulin use, oral hypoglycemic use, or a fasting glucose ≥ 126 mg/dL. Hypercholesterolemia was defined as total serum cholesterol > 240 mg/dL, a patient's self-report of hypercholesterolemia or the presence of lipid-lowering treatment. Cigarette smoking was defined by a current history of cigar or cigarette smoking (smoking within a year). Body mass index was calculated as weight (kilograms) divided by height (meters) squared. The presence of atrial fibrillation was documented based on the results of a current or past ECG. Coronary artery disease included history of myocardial infarction or typical angina or the patient's reporting of a positive diagnostic test (stress test, coronary angiography) or drug treatment. Carotid duplex Doppler examination to assess for stenosis was performed in 216 stroke patients (84.7%) and in 168 control subjects (80%).

The method for assessment of AP has been described fully in previous publications.(20) Briefly, transesophageal echocardiography was performed with an Agilent 2500, 4500, or 5500 system with a 5MHz omniplane transducer. AP in proximal thoracic aorta (i.e., proximal to the takeoff of the left subclavian artery) was assessed by a single experienced echocardiographer (MDT) blinded to the subject's risk factors. AP thickness was measured in the horizontal plane, perpendicular to the major axis of the aortic lumen as previously reported.(20) AP was deemed present when its thickness was equal to or more than 2 mm. Large AP was defined thickness equal to or greater than 4 mm. This cutoff has been shown to correlate with risk of stroke in prior studies(14) and is generally accepted as clinically relevant (14–18). The presence of plaque ulcerations and/or superimposed mobile components was also recorded. Echocardiographers performing the TEE were blinded to subject's lipid parameters and other risk factors.

Statistical Analysis

The distributions of lipid parameters and other variables were examined. Differences between mean values were assessed by Student's t-test, between proportions by chi-square test. Univariate and multivariate logistic regression analyses were performed to test the association between lipid parameters and any AP or large AP before and after adjustment for potentially confounding cardiovascular risk factors (age, sex, hypertension, diabetes, and cigarette smoking). The lipid parameters that were significantly associated with the presence of any AP were categorized into quartiles, and association between the presence of AP and the highest quartile (vs. lowest) of the lipid parameter distributions was analyzed. The same analyses were performed for stroke patients and control subjects separately. Statistical significance was determined at the $\alpha=0.05$ level with 2-sided tests. Statistical analyses were performed with SAS 9.1 computer software (SAS Institute).

Results

Baseline Characteristics

We enrolled 464 subjects (251 male, 213 female), including 255 patients with first ischemic stroke and 209 stroke-free controls matched to cases by age, sex and race-ethnicity. Participants were predominantly male (54.1%), elderly (mean age 69.1 ± 9.0) and hypertensive (76.3%) (Table 1). The prevalence of hypercholesterolemia, diabetes, and smoking were 44.2%, 33.3%, and 17.4%, respectively. Atrial fibrillation was present in 8.6% of our cohort. Carotid stenosis $\geq 60\%$ was more frequent in stroke patients than in control subjects, as were many of the cardiovascular risk factors (Table 1). Only one control subject (0.6%) had evidence of carotid stenosis $>60\%$ by Doppler ultrasound. The etiology of stroke was thought to be lacunar in 61 patients (23.9%), atherosclerotic in 51 patients (20.0%), cardioembolic in 44 (17.2%). A stroke of unknown cause (cryptogenic) was diagnosed in 92 of 255 stroke patients (36.1%).

Overall, AP of any thickness was detected in 326 subjects (70.4%); 174 subjects (37.6%) had large AP ($\geq 4\text{mm}$), 67 subjects (14.5%) had ulcerated or mobile AP and 5 subjects (1.1%) had both of these characteristics. Subjects with AP were older (71.0 ± 9.0 vs. 64.6 ± 7.2 , $p < 0.001$), more likely to smoke (19.9% vs. 11.4%, $p = 0.029$), and to have hypercholesterolemia (47.7% vs. 36.6%, $p = 0.028$) and coronary artery disease (15.5% vs. 5.8%, $p = 0.004$). The number of subjects who had significant carotid stenosis ($\geq 60\%$) increased as degree of AP progressed. The prevalence was 3.6%, 7.5% and 10.9% for subjects with no AP, any AP and large AP, respectively ($p = 0.15$ for AP vs. no AP, and $p = 0.006$ for large AP vs. no AP).

Predictors of Any AP and Large AP ($\geq 4\text{mm}$)

After adjustment for major cardiovascular risk factors (Table 2), HDL and Apo B/A-I ratio emerged as the strongest predictors of any AP, followed by individual Apo B and A-I levels, TG and non-HDL level. Only HDL and Apo A-I ratio were significant predictors of large AP ($\geq 4\text{mm}$). The association patterns for these lipid parameters and AP or large AP ($\geq 4\text{mm}$) showed similar trend when stroke patients and control subjects were analyzed separately (Table 3); HDL and non-HDL cholesterol were significant predictors of any plaque in stroke patients. HDL and Apo A-I levels trended for prediction of large plaque in controls but did not reach statistical significance. Small sample size (53 out of 209) prevented the calculation for Apo B/A-I ratio in controls.

The two parameters that had the strongest association with AP in the overall study group (HDL and Apo B/A-I ratio) were categorized into quartiles and the association between each quartile and the presence of any AP was evaluated. The adjusted OR for any AP for the highest quartile of HDL (vs. lowest quartile) was 0.33 (95% CI 0.17–0.67, $p = 0.002$). Compared to the lowest quartile, the second and third quartiles were not significant predictors for any AP. For Apo B/A-I ratio, the adjusted OR for any AP in the highest quartile (vs. lowest quartile) was 4.05 (95% CI 1.05–10.9, $p = 0.006$), and the adjusted OR for any AP in second and third quartile (vs. lowest quartile) was 2.71 (95% CI 1.21–6.07, $p = 0.016$).

Analysis Excluding Subjects on Cholesterol-Lowering Agents

Drug information was available in 388 subjects, and 84 of them (21.6%) were on cholesterol-lowering agents. We conducted a separate analysis on the 304 subjects who were not on cholesterol-lowering treatment. Two-hundred forty-nine subjects (69.1%) had AP of any thickness and 130 subjects (34.3%) had large AP. The HDL cholesterol level remained

significant predictor for any AP and large AP (Table 4). Triglycerides, Apo B and Apo B/A-I ratio predicted the presence of any AP but not large AP.

Discussion

This is the first study to assess lipid risk factors for AP in an elderly cohort that included both stroke patients and normal volunteers. Our results support a previously described association between atherosclerosis and the cholesterol balance determined as HDL or alternatively as Apo B/A-I ratio, and extends that observation to the aortic arch, a region of particular interest for its potential for embolism to the brain. These associations were present independently of other traditional atherosclerotic risk factors, including age, sex, hypertension, diabetes, and smoking, and were also demonstrated in a subgroup that excluded patients on cholesterol-lowering therapy, a potential confounder of the association between lipid parameters and aortic atherosclerosis. There were both a continuous relationship of HDL and Apo B/A-I ratio with AP thickness and an association with AP thickness of ≥ 4 mm, a thickness cutoff that strongly correlates with risk of stroke.(14) Moreover, there was a dose-response relationship between quartiles of Apo B/A-I ratio and HDL cholesterol and AP presence, further reinforcing the strength of the finding.

Previous small echocardiographic studies addressing the association between lipid parameters and aortic atherosclerosis yielded discordant results. An association between LDL (but not HDL) and aortic atherosclerosis has been occasionally observed(21) but not confirmed in other studies.(22,23) This discordance is probably due to different patient selection, as patients referred to TEE for various clinical reasons were included. In contrast, the APRIS study enabled us to assess stroke patients and a sample of the general population, and demonstrated strong and significant association between AP and HDL but not LDL. Also, this study confirmed the inadequacy of total cholesterol levels as indicators of the atherosclerotic burden.

Both clinical observations and basic laboratory experiments support the hypothesis that HDL is antiatherogenic(24) and has both direct and indirect anti-inflammatory effect that may effectively translate into antithrombotic activities.(25) A recent longitudinal study demonstrated that a high level of HDL cholesterol reduces plaque growth in subjects with preexisting carotid atherosclerosis,(26) which is in accordance with our observation. However, over half of our patients had an ischemic stroke, and this might have been at least a partial confounder in the relationship between HDL and aortic atherosclerosis, since tissue inflammation and caloric deficit in these patients can reduce HDL after stroke.(27) We found, however, that there was a significant association between any aortic atherosclerosis and HDL levels even when the stroke patients and controls were analyzed separately.

Given the strong negative association of AP and HDL, our results indicate that low levels of HDL deserve special attention in clinical practice in patients who have significant risk factors for stroke, and that HDL levels may be better targets for treatment strategies than LDL cholesterol in patients with AP.(28) Pharmacological elevation of HDL-cholesterol is considered to be a promising strategy for achieving further reductions in cardiovascular risk in statin-treated patients(29) although initial experiences in the ILLUMINATE Study did not show benefits with a CETP inhibitor.(30) Another potential HDL-raising drug is nicotinic acid, and this agent has been shown to reduce coronary events in the Coronary Drug project and slow progression of atherosclerosis.(31) However, it has not been tested in reducing strokes or aortic disease.

The evidence for the Apo B/A-I ratio as a strong new risk factor for cardiovascular disease is increasing.(9,10) The apolipoproteins tend to remain stable with age and severity of

disease, whereas lipoproteins such as LDL and HDL tend to decrease over time. A large-scale cross sectional study in asymptomatic young individuals demonstrated the strong correlation of apolipoproteins with carotid intima-media thickness, and their superior prognostic value for predicting cardiovascular events.(32,33) However, studies comparing the utility of apolipoprotein with lipoprotein measurements in detecting subclinical atherosclerosis have been limited. Furthermore, data on risk factors for AP is less readily available. No previous large studies have reported a positive association between apolipoprotein fractions and aortic atheromas. In the present study, Apo B/A-I ratio emerged as the strongest predictors of aortic atherosclerosis, and both individual Apo B and A-I levels were also significantly associated with presence of aortic plaques.

Increased levels of triglyceride-rich lipoproteins are known to be associated with low levels of HDL. In patients with carotid stenosis, increased triglyceride-rich lipoproteins (but not LDL) and reduced HDL correlated strongly with presence of echolucent, rupture-prone plaques.(34,35) Elevated triglycerides level is also a component of the metabolic syndrome, and trends toward higher triglyceride levels have been reported in patients who subsequently experience ischemic stroke.(36–38) However, triglyceride levels vary considerably, making it difficult to evaluate them as a risk factor for stroke. In our study, triglycerides levels showed significant association with any AP, but not with large AP.

A recent study has shown that statin therapy reduces AP progression, accompanied by a reduction in total cholesterol and LDL, but not with changes in HDL. (39) Another study showed no difference in total cholesterol, LDL, HDL or triglycerides between stroke patients with or without progression of AP. (40) We conducted a separate analysis on patients who were free of cholesterol lowering medications, and HDL cholesterol level remained a significant predictor for both any AP and large AP. The effect of conventional cholesterol treatment on AP remains to be further investigated.

Limitations

Because of their small number, we could not consider complex atheromatous plaques (i.e., ulcerated or mobile plaques) as a dependent variable in the analysis. In addition, different stroke subtypes (i.e., cryptogenic vs. known cause) could not be individually analyzed. Furthermore, our subanalyses on stroke and control subjects are limited due to small number of subjects, as reflected in wide confidence intervals. Therefore, we avoided drawing any significant conclusions relying on the results of these subanalyses.

Our control subjects were questioned on neurological symptoms and signs to assure stroke-free status on enrollment in the study, but head MRI was not performed at enrollment. Therefore, asymptomatic brain infarcts could not be considered in the analysis. Finally, due to the cross-sectional design of our study, the association between Apo B/A-I ratio or HDL and AP does not imply a causal relationship. The actual relationship between Apo B/A-I ratio or HDL and atherosclerosis remains to be determined from large-scale prospective studies.

Conclusions

In summary, our study supports the role of HDL cholesterol, and alternatively ApoB/A-I ratio, as predictors of proximal aortic arch atherosclerosis. Further studies are necessary to explore the hypothesis that targeted therapies may decrease the risk of events in this patient population.

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Table 1

Baseline patient characteristics of the APRIS study population.

Clinical Variables	All Subjects <i>n</i>=464	Stroke Patients <i>n</i>=255	Control Subjects <i>n</i>=209	<i>p</i>-value
Male (%)	54.1	52.2	56.5	0.35
Age (yr)	69.1±9.0	70.9±9.0	67.0±8.6	<0.001
Atrial fibrillation (%)	8.6	11.6	5.3	0.02
Diabetes (%)	33.3	42.4	22.5	<0.001
Hypertension (%)	76.3	85.7	65.1	<0.001
Coronary artery disease (%)	12.6	17.1	7.2	0.001
Hypercholesterolemia (%)	44.2	40.3	48.8	0.069
Cigarette smoking (%)	17.4	18.4	16.1	0.51
Carotid stenosis ≥60% (%)	5.4%	11.1	0.6	<0.001
Any AP (≥2mm) (%)	70.4	77.2	62.2	<0.001
AP less than 4mm (%)	26.3	28.4	38.1	0.02
Large AP (≥4mm) (%)	37.6	48.8	23.9	<0.001
Ulcerated AP (%)	14.0	25.5	6.2	<0.001
Ulcerated Large AP (%)	13.8	20.5	5.7	<0.001
Lipid Parameters				
Total Cholesterol (mg/dl)	190.7±40.3	187.2±43.1	194.3±37.0	0.07
Triglycerides (mg/dl)	130.3±71.7	134.2±61.7	126.3±80.8	0.262
HDL Cholesterol (mg/dl)	42.9±13.6	40.3±13.5	45.5±13.3	<0.001
LDL Cholesterol (mg/dl)	122.0±36.0	119.8±37.1	124.3±34.8	0.204
Non-HDL Cholesterol (mg/dl)	147.7±39.6	146.6±41.3	148.8±37.8	0.569
Lipoprotein (a) (mg/dl)	58.7±40.0	63.0±42.3	53.7±36.7	0.066
Apolipoprotein B (g/l)	98.9±26.8	99.8±29.0	98.1±24.7	0.561
Apolipoprotein A-I (g/l)	127.4±27.9	119.3±31.3	134.7±20.0	<0.0001
Apolipoprotein B to A-I ratio	0.86±0.27	0.88±0.29	0.80±0.22	0.067

AP=aortic atherosclerotic plaque

Table 2

Variables associated with aortic plaque - multivariate analysis results.

	All Subjects n=464					
	Any AP (≥2mm)			Large AP (≥4mm)		
	OR [†]	95%CI	P-value	OR [†]	95%CI	P-value
Total Cholesterol	1.003	0.997–1.009	0.273	1.000	0.995–1.006	0.957
Triglycerides	1.004	1.000–1.008	0.027*	1.001	0.998–1.004	0.457
HDL Cholesterol	0.970	0.954–0.988	<0.001*	0.977	0.970–0.994	0.008*
LDL Cholesterol	1.006	0.999–1.012	0.081	1.002	0.996–1.008	0.488
Non-HDL Cholesterol	1.007	1.001–1.013	0.021*	1.003	0.997–1.008	0.309
Lipoprotein (a)	1.002	0.995–1.010	0.541	1.001	0.994–1.008	0.845
Apo B	1.013	1.002–1.023	0.015*	1.007	0.998–1.016	0.137
Apo A-I	0.988	0.978–0.998	0.016*	0.986	0.977–0.996	0.006*
Apo B/A-I	7.981	1.950–32.64	0.004*	2.699	0.848–8.596	0.093

OR=odds ratio, HDL=high density lipoprotein, LDL=low density lipoprotein, Apo B/A-I=apolipoprotein B to A-I ratio

[†] Adjusted by age, gender, hypertension, diabetes and current smoking

* indicates p-value <0.05

Table 3
Variables associated with aortic plaque - subgroup analysis for stroke patients and control subjects.

	Stroke Patients n=255					
	Any AP (≥2mm)			Large AP (≥4mm)		
	OR [†]	95%CI	P-value	OR [†]	95%CI	P-value
Total Cholesterol	1.004	0.996–1.012	0.319	1.001	0.994–1.008	0.785
Triglycerides	1.006	0.999–1.014	0.070	1.001	0.996–1.006	0.799
HDL Cholesterol	0.957	0.931–0.984	0.002*	0.988	0.966–1.011	0.308
LDL Cholesterol	1.009	1.00–1.019	0.062	1.003	0.995–1.011	0.504
Non-HDL Cholesterol	1.010	1.001–1.019	0.030*	1.003	0.995–1.010	0.497
Lipoprotein (a)	1.003	0.993–1.014	0.550	0.998	0.989–1.007	0.637
Apo B	1.015	0.999–1.031	0.073	0.998	0.986–1.011	0.785
Apo A-I	0.988	0.974–1.002	0.090	0.993	0.981–1.005	0.265
Apo B/A-I	4.316	0.919–20.3	0.064	1.135	0.332–3.887	0.840

	Control Subjects n=209					
	Any AP (≥2mm)			Large AP (≥4mm)		
	OR [†]	95%CI	P-value	OR [†]	95%CI	P-value
Total Cholesterol	1.001	0.993–1.01	0.74	0.997	0.987–1.006	0.487
Triglycerides	1.003	0.999–1.007	0.205	1.001	0.997–1.006	0.478
HDL Cholesterol	0.984	0.96–1.009	0.204	0.975	0.947–1.003	0.08
LDL Cholesterol	1.002	0.993–1.011	0.694	0.998	0.988–1.008	0.641
Non-HDL Cholesterol	1.003	0.995–1.012	0.445	1.00	0.991–1.009	0.952
Lipoprotein (a)	0.997	0.984–1.009	0.60	0.999	0.986–1.012	0.869
Apo B	1.008	0.994–1.022	0.263	1.011	0.996–1.027	0.156
Apo A-I	0.991	0.975–1.006	0.241	0.984	0.966–1.002	0.074
Apo B/A-I	- §			- §		

OR=odds ratio, HDL=high density lipoprotein, LDL=low density lipoprotein, Apo B/A-I=apolipoprotein B to A-I ratio

[†] Adjusted by age, gender, hypertension, diabetes, current smoking

* indicates p-value <0.05

§ small sample size (53 out of 209) prevented the calculation

Table 4

Variables associated with aortic plaque - multivariate analysis results.

	Subjects Not On Cholesterol-Lowering Agents n=304					
	Any AP (≥ 2 mm)			Large AP (≥ 4 mm)		
	OR [†]	95%CI	P-value	OR [†]	95%CI	P-value
Total Cholesterol	1.005	0.998–1.012	0.162	1.003	0.996–1.009	0.449
Triglycerides	1.006	1.001–1.011	0.019*	1.002	0.998–1.005	0.391
HDL Cholesterol	0.971	0.949–0.994	0.012*	0.973	0.952–0.996	0.018*
LDL Cholesterol	1.008	0.999–1.016	0.076	1.005	0.997–1.013	0.198
Non-HDL Cholesterol	1.009	1.002–1.017	0.019*	1.006	0.999–1.013	0.108
Lipoprotein (a)	1.004	0.994–1.013	0.459	0.999	0.990–1.008	0.823
Apo B	1.014	1.000–1.028	0.043*	1.010	0.998–1.022	0.115
Apo A-I	0.990	0.978–1.003	0.144	0.992	0.980–1.003	0.164
Apo B/A-I	7.18	1.207–42.7	0.030*	2.73	0.621–12.0	0.183

OR=odds ratio, HDL=high density lipoprotein, LDL=low density lipoprotein, Apo B/A-I=apolipoprotein B to A-I ratio

[†] Adjusted by age, gender, hypertension, diabetes and current smoking

* Indicates p-value <0.05